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specific expression using the promoter of cancelled Claim 5. No new matter has been added.

Turning now to the Official Action, the Examiner rejected Claims 5 and 6 under 35 U.S.C. §101 as the claimed invention is purportedly directed to non-statutory subject matter. Applicants have cancelled Claim 5 and amended Claim 6 to recite an "isolated potato gene." In light of these amendments, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 1 and 4-20 under 35 U.S.C. §112, second paragraph, as being purportedly indefinite.

Specifically, the Examiner rejected Claims 1, 4-8 and 10 (and Claims 9 and 11-20 which are dependent thereon) for the recitation of "essentially. This portion of the rejection is respectfully traversed. It is known in the art that a certain deviation from a given sequence will still give the same result. This fact is reflected in the use of the term "essentially," which is specifically objected to by the Examiner. It is well known that during the isolation of the gene and also in the assembling of the gene constructs there might occur minor variations in the DNA sequence. Furthermore, the gene from different potato varieties may differ without influencing the function of the gene. The term "essentially" reflects the requirement that the claimed sequences should have the same function as the sequences in the SEQ ID NOS. This language finds support in the specification at least at page 6, lines 5-10 and lines 15-20.

The Examiner also rejected Claims 1, 4, 7 and 9-10 for improper Markush group terminology. These claims have been amended to correct the Markush terminology. The Examiner also rejected Claims 4-7 and 10 (and Claims 8-9 and 11-20,

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dependent thereon) for the recitation of "in potato." These Claims have been amended to recite "potato gene" rather than "in potato." The Examiner also rejected Claim 10 for the recitation of "antisense orientation." Claim 10 has been amended to recite that the gene is in the antisense orientation in relation to the promoter. In light of the foregoing remarks and amendments, withdrawal of the rejection under 35 U.S.C. §112, second paragraph is respectfully requested.

The Examiner also rejected Claims 5-6 under 35 U.S.C. §102(a) or 102(b) as being anticipated by Rohde et al. This rejection, to the extent it applies to Claim 6, as amended, is respectfully traversed.

Submitted herewith is a letter from the publisher of the journal in which Rohde et al appeared (with an English translation thereof) confirming that the issue in which Rohde et al appeared was given to the Post Office for delivery on January 18, 1991, well after the priority date of the present application, which is December 21, 1990.

The publisher also enclosed two notes with his letter, which he says could be of interest. As can be seen, these notes concern a delivery of some gene sequences to a data bank on April 9, 1990. However, the two sequences concerning fragments of *S. tuberosum*, merely depict the sequences for two promoters, G28 and G1, respectively, without any further information regarding the use of the sequences or the sequences of the rest of the genes, and certainly no mention or suggestion of the use of certain coding parts of the genomic clone in an antisense direction for inhibiting the formation of amylose in potato. In support thereof, also enclosed are copies of the information in the data bank. Although Applicants have not been able to verify whether this information is exactly the same as that entered in April 1990, since the sequences of the promoters are

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the same as those in the publication from January 1991, Applicants assume that the now available data are the same as filed in April 1990.

From the publication in the data bank (delivered in April 1990) only the sequence of the promoter is given, that is, the sequence according to SEQ ID No. 4, and those parts of the sequence according to SEQ ID No. 5 comprising the promoter sequence. Applicants have now added new Claim 21, which recites a method of "using of an isolated promoter for the potato gene for granule-bound starch synthase (GBSS), having essentially the nucleotide sequence stated in SEQ ID No. 4, for tuber specific expression." The information in the data bank in no way discloses or suggests using these sequences for such a method.

Also enclosed are a certified copy of the priority document together with a certified translation thereof. In light of the submission of these documents, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 5-6 under 35 U.S.C. §102(a) as being purportedly anticipated by van der Liej et al. In light of the submission of the priority document and translation perfecting Applicants' claim for priority, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 5-6 under 35 U.S.C. §102(b) as being purportedly anticipated by Visser or Visser et al (1989). This rejection, to the extent it applies to Claim 6, as amended, is respectfully traversed.

Neither Visser nor Visser et al disclose any DNA sequence whatsoever. Moreover, Visser was not able to link the isolated gene to the amf-mutant (high in amylopectin). It is known in the art that in pea, rice and maize there are several forms of

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one and the same enzyme. Therefore it cannot be a certainty that Visser's isolated gene is the same as the gene claimed by the present application. Furthermore, a recent publication by Dry et al (submitted herewith), describes both a GBSSI and a GBSSII gene in potato. This publication supports Applicants' position that there is no proof of Visser's isolated gene being the same as the gene claimed in the present application. The fact that full length genomic clones inherently include the promoter does not anticipate the isolated promoter.

In addition, because neither Visser or Visser et al disclose any sequence information, the location of the promoter within Visser's genomic clone cannot be determined. Thus, both Visser and Visser et al give no guidance on isolation of the promoter from the full-length genomic clone. In light of the foregoing, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 14, 16 and 20 under 35 U.S.C § 102(b) as being purportedly anticipated by or, in the alternative, under 35 U.S.C §103 as being purportedly obvious over Hovenkamp-Hermelink et al. This rejection, to the extent it applies to the claims, as amended, is respectfully traversed.

Applicants note that the claimed amylose-free tubers and microtubers are provided by genetic engineering. Hovenkamp-Hermelink et al describes isolation of an amylose-free starch mutant of potato. There is no disclosure or suggestion related to inactivation of the GBSS gene in the document. The cited paragraph (page 220, column 2, first full paragraph) states that the amylose-free variant of potato described by Hovenkamp-Hermelink et al is characterized by the absence of GBSS and is therefore analogous to waxy maize. Thus, one could not deduce from this document that a means

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of obtaining an amylose-free potato would be to inhibit the expression of the GBSS gene by inserting a special gene fragment in an antisense direction. In fact, it has only been the work by the present inventors which has made it possible to reproducibly and predictably produce amylose-free potato tubers.

Moreover, Hovenkamp-Hermelink et al have had problems due to the mutant not being stable, probably because their plants have been chimeras. Thus, the plant of Hovenkamp-Hermelink et al is not agriculturally valuable, while the genetically new material of the present application has been directly introduced into plants to produce an agriculturally valuable material. In light of the foregoing, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 13-15 and 19-20 under 35 U.S.C. §102(b) as being purportedly anticipated by or, in the alternative, under 35 U.S.C. §103 as being purportedly obvious over Cochran. This rejection, to the extent it applies to the claims, as amended, is respectfully traversed.

Cochran teaches a potato variety having certain characteristics. There is no disclosure or suggestion of an amylose-free potato comprising the claimed gene construct. As already stressed above, there is a great difference between such a known potato variety and the presently claimed potato plants and tubers, in that the latter comprise the claimed gene construct which results in the tubers containing mainly amylopectin starch.

In support of the statements in the specification regarding providing an amylose-free potato starch, submitted herewith is a summary from the inventors of a characterization of genetically modified starch of amylopectin-type. Note that "GMS of amylopectin-type" is the genetically modified potato starch of amylopectin-type as

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recovered from the potato tubers according to the invention. The information contained in the summary will be incorporated into a Declaration Pursuant to 37 C.F.R. §1.132 to be signed by one of the present inventors, and will be submitted with a Supplemental Response as soon as it is received by the undersigned.

The Examiner also rejected Claim 16 under 35 U.S.C. §102(b) as being purportedly anticipated by or, in the alternative, under 35 U.S.C. §103 as being purportedly obvious over Twell et al. This rejection, to the extent it applies to the claims, as amended, is respectfully traversed.

Applicants note that the same arguments made above regarding the rejection of Claims 13-15 and 19-20 can also be made regarding the rejection of Claim 16. Thus, a significant difference between the claimed microtubers and the potato microtubers of Twell et al lies in the fact that the latter do not comprise the claimed antisense construct. Again, the enclosed test results discuss the difference between starch from ordinary potato tubers and the "amylopectin potato" tubers according to the present invention. Thus, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 1, 4, 7 and 9-16 under 35 U.S.C. §103 as being purportedly unpatentable over Visser. This rejection, to the extent it applies to the claims, as amended, is respectfully traversed.

Visser uses constructs carrying antisense maize GBSS sequences. The maximal reduction in amylose content of reserve starch attained with this method was 29%. Not all plants transformed with the same antisense construct showed the same response (see the summary of Chapter 6).

The results described in this chapter were never published in any scientific

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journal, as they appeared to be confusing and inconsistent. Thus, this chapter cannot teach one skilled in the art a useful way of inhibiting amylose formation in potato tubers. This is supported by the following:

- Page 104: "PAS transformed hairy roots showed staining results, which were hardly ever observed in PBI121 transformed or untransformed roots during growth." This is more an indication of a subjective frequency observation than a real difference between antisense-transformed material and control.

- Pages 104-105: The variations shown are based on a small quantity of material. Further, the measurements are made on minituber, which indicates the use of immature material which is impossible to compare in a scientifically correct way. There is information in the literature on the variation of the amylose-amylopectin ratio in immature material.

- Page 107: The figure which is meant to show how much of GBSS protein the antisense-transformants contain compared to the control does not in fact demonstrate anything at all. The amount of GBSS protein in an antisense-transformant is 50% higher at the same time as the activity is lowered by 75%. A mean value for the PAS transformants is approximately the same as the value for the control.

- Pages 109-110: From these pages it is very clear that Visser is unable to demonstrate that he has lowered the content of the protein which is missing in the amf mutant.

- Page 111: "The rather small reduction in the amylose/amylopectin ratio associated with a strong reduction in GBSS activity could point to the involvement of a second enzyme capable of amylose synthesis."

- Page 112: "... in minituber- or roottip-starch from PAS transformants: all starch stained blue." Compare Visser's use of iodine staining as a means of separating antisense transformant and control.

Chapter 7 of Visser's thesis: "Summary and general conclusions":

Visser has not in any way been able to demonstrate a connection between what he calls the GBSS gene and the GBSS protein. What Visser calls the GBSS gene is also expressed in the amf mutant. He also admits this fact on page 120: "The absence of amylose and the GBSS protein does not necessarily mean that a mutation in the GBSS gene is involved: a mutation in another gene, although not known in the literature, might achieve a similar phenotype." and further: "Another, more conclusive way to investigate whether the mutation lies within the GBSS gene is to perform complementation experiments." but (page 121): "Attempts to complement the mutant with a potato GBSS CDNA construct..... gave no positive result."

In the bottom paragraph on page 122 Visser speculates on what new knowledge (not provided by his theses) might lead to. Having in mind the above analysis of what is taught by Visser's theses, and the summary by the Examiner of the alleged obviousness on page 9 of the Official Action, based on a combination of 5 different points which have to be put together in order to arrive at the claimed invention, it is a clear hindsight to draw the conclusion that the claimed invention would have been obvious for the man skilled in the art.

In further support of Applicants' argument, there are several documents pointing to the existence of several genes and enzymes, e.g. Smith "Evidence that the "waxy" protein of pea (*Pisum sativum* L.) is not the major starch-granule-bound starch

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synthase" (copy submitted herewith). In light of the above discussion, it is Visser cannot render the present invention obvious, because there was absolutely expectation of successfully using Visser's method, which was not very effective in m. to transform potato to get amylose-free tubers and microtubers. Thus, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 8 and 17-20 under 35 U.S.C. §103 as being purportedly unpatentable over Visser as applied to Claims 1, 4, 7 and 9-16, and further in view of Rohde et al. Applicants maintain that this rejection is moot in light of the above arguments together with the confirmation of the inventors' priority rights. However, in this context, Applicants would like to point to an error appearing in the Examiner's statement, that is Visser does not teach a gene construct comprising the potato GBSS gene in antisense orientation but the maize GBSS gene (cf. the last 5 lines on page 8 of the Official Action). Thus, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 8 and 16-20 under 35 U.S.C. §103 as being purportedly unpatentable over Visser as applied to Claims 1, 4, 7 and 9-16, and further in view of Twell et al. This rejection is respectfully traversed.

Applicants note that the same error appears regarding what is taught by Visser. Having demonstrated above that Visser does not teach the antisense construct according to the present invention, the teaching by Twell et al that the 5' flanking DNA of a patatin gene directs tuber specific expression of a chimeric gene in potato cannot make the claimed invention obvious. Thus, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 1, 4, 7 and 9-15 under 35 U.S.C. §103

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as being purportedly unpatentable over Visser et al (1991). In light of the submission of the present application's priority document and its translation, Visser et al (1991) cannot be applied as a reference. Thus, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 8 and 16-20 under 35 U.S.C. §103 as being purportedly unpatentable over Visser et al (1991) as applied to Claims 1, 4, 7 and 9-15 above, and further in view of Twell et al. In light of the submission of the present application's priority document and its translation, Visser et al (1991) cannot be applied as a reference. Twell et al is discussed above. Thus, withdrawal of this rejection is respectfully requested.

The Examiner also rejected Claims 8 and 17-20 under 35 U.S.C. §103 as being purportedly unpatentable over Visser et al (1991) as applied to Claims 1, 4, 7 and 9-15 above, and further in view of Rohde et al. In light of the submission of present application's priority document and its translation, neither Visser et al (1991) nor Rohde et al can be applied as a reference. Thus, withdrawal of this rejection is respectfully requested.

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

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In the event that there are any questions concerning this Amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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